

REMARKS

Applicants respectfully request reconsideration of this application in view of the following remarks. Applicants gratefully acknowledge the Examiner's entry of applicants' amendment filed on September 10, 2001. Applicants also gratefully acknowledge the Examiner's withdrawal of (1) the rejection of claims 1-11 under 35 U.S.C. § 112, first paragraph; and (2) the rejection of claims 1-3, 5-11, 22 and 25-28 under 35 U.S.C. § 103(a).

Rejections Under § 102(b)

Certain of the currently pending claims stand rejected under 35 U.S.C. § 102(b) in view of several references that show the use of IVIG in treating secondary infections in patients who also have lymphoma. None of the cited references, however, indicate that the lymphoma is metastatic or capable of metastasis. Each of applicants' pending claims requires the use of IVIG or fragments thereof in the inhibition of lymphoma metastasis or treatment of metastatic lymphoma. Such methods are not inherently performed by the prior art.

Chapel et al.

The Examiner has rejected claims 1-2, 7-9 and 25-28 under 35 U.S.C. § 102(b) based on Chapel et al.* The Examiner contends that the administration of IVIG in

* Chapel et al., "A Crossover Study Of The Use Of Intravenous Immunoglobulin For Prophylaxis Against Infection In Patients With Chronic Lymphocytic Leukemia Or Low Grade
(continued...)

Chapel et al. inherently inhibits the metastasis of the lymphoma. As applicants have stated previously, however, there is no indication in Chapel et al. that the lymphoma in question was of a metastatic nature -- nothing about metastasis in this study can be inferred one way or the other.

The Examiner points to the definitions of “metastasis” and “inhibition of metastasis” in the specification as support for the proposition that Chapel et al. inherently prevented or reduced the development of metastases. The Examiner’s argument assumes that the patients in Chapel et al. had metastatic lymphoma, *i.e.*, the lymphoma was of a type that was capable of metastasizing or was in fact metastasizing, and was therefore subject to “inhibition of metastasis” through administration of IVIG as defined in the instant application. This is not a valid assumption. The non-Hodgkin’s lymphoma described in Chapel et al. could have been metastatic or non-metastatic – each scenario is possible and plausible. If there was no metastasis present or none capable of occurring, then no inhibition of metastasis can have taken place at the time of IVIG administration, and no inherent anticipation can have occurred, because each of the rejected claims requires the inhibition of metastasis or treatment of metastatic lymphoma. One cannot assume that metastatic lymphoma was present in Chapel et al. based on probability or possibility. The Examiner states that “[c]ontrary to Applicants’ assertions, no requirement for active metastasis is necessary.” There is, however, a requirement for lymphoma with the capacity for metastasis

* (...continued)
Non-Hodgkins Lymphoma,” Clin. Res. 36, pp. 407A (1988).

or actual metastasis at the time of the administration of IVIG by Chapel et al. There is no unambiguous evidence that this is the case.

The Examiner also states that “the claims do not require the added step of first determining [if] the lymphoma has metastatic potential, only inhibiting the metastasis of the lymphoma, which is accomplished by the addition of IVIG, exactly as disclosed by Chapel et al.” It is true that the claims do not require the step of determining whether the lymphoma has metastatic potential, yet by virtue of the metastatic lymphoma limitation, an anticipatory reference must unambiguously carry out the administration of IVIG to patients with lymphoma that is capable of metastasizing or actually metastasizing at the time of the administration of IVIG. In order to meet his burden of showing that the prior art contains every element of the claims, the Examiner is required to show that the lymphoma of the prior art has such metastatic potential.

Rapoport v. Dement, confirms that inherency may not be established by probabilities or possibilities. In Rapoport, the Court held that a count claiming a “method of treating sleep apneas” was not anticipated by a prior art reference treating symptoms of sleep apneas, where no evidence was presented that the prior art reference actually treated the underlying respiratory disorder. The Court warned against making certain “speculative assumptions” in determining inherency, reiterating that “[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing **may** result from a given set of circumstances is not sufficient” Rapoport v. Dement, 59 USPQ2d 1215, 1222 (Fed. Cir. 2001) (emphasis in original) (citations omitted).

Similarly, here, each of the prior art references cited by the Examiner for anticipation only show IVIG treatment of secondary infections or symptoms **other** than metastasis of lymphoma. There is no disclosure in the cited references of the use of IVIG in patients with metastatic lymphoma. In each case, it is possible that IVIG treatment was carried out in patients having a primary tumor only, and that such a tumor was, at the time of administration of IVIG, incapable of metastasis and not actively metastatic. In such a case, administration of IVIG would not function to prevent, inhibit or treat metastasis, because no potential or actual metastasis existed at that time.

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. Rapoport at 1218 (citation omitted). Here, the cited references do not disclose every limitation of the claimed invention. The cited references do not inherently disclose inhibition of metastasis of lymphoma or treatment of metastatic lymphoma, because the assumption cannot be made that the lymphoma described in the cited references was in fact metastatic or had the potential to become metastatic as of the time of administration of IVIG.

As stated by the Federal Circuit in In re Derwood L. Runion, “if the crucial property or characteristic of the reference is not necessarily implicit in the reference’s disclosure, then the principles of inherency do not apply and a reference without either inherent or explicit disclosure of each and every element of the claim cannot anticipate the

claim.” In re Derwood L. Runion, 1993 U.S. App. LEXIS 1945 (Fed. Cir. 1993).^{*} Here, “metastatic lymphoma” is not necessarily implicit in the cited references’ disclosure of various lymphomas. Thus, the cited references do not inherently disclose inhibition of metastasis of lymphoma or treatment of metastatic lymphoma by IVIG.

The Examiner’s statement that “[a]dministering the IVIG to an individual with non-Hodgkin’s lymphoma results in the inhibition of metastasis” is not necessarily true. The possibility exists that, at the time of IVIG administration, the non-Hodgkin’s lymphoma was neither metastatic nor capable of metastasis. Therefore, no inhibition of metastasis could occur at that time. Without certain proof that the lymphoma in Chapel et al. was metastatic or capable of metastasis, Chapel et al. cannot be deemed to anticipate applicant’s invention.

The Examiner’s analogy to administration of an antibiotic does not shed light on the instant case. The Examiner states that “administration of an antibiotic results in the inherent inhibition of bacterial infection, regardless of whether or not a bacterial microorganism is present or not.” Applicants disagree with this statement. Without a bacterial organism for an antibiotic to act upon, there can be no inhibition of bacterial infection. According to this example, if a prior art reference taught the administration of an antibiotic to a mammal when no bacterial infection was present in the mammal, that prior art

* Though an unpublished and therefore non-precedential case, applicants believe that the cited language is representative of the Federal Circuit’s view of the inherency doctrine. The quoted passage was the Court’s conclusion regarding inherency based on a citation from Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264 (Fed. Cir. 1991).

reference could not be deemed to anticipate a claim directed to the inhibition of bacterial infection – the temporal disconnect precludes it. For the prior art reference to anticipate such a claim, administration of the antibiotic in the prior art would have had to coincide with the bacterial infection such that inhibition of infection could occur.

Thus, applicants respectfully request that the Examiner withdraw the rejection of claims 1-2, 7-9 and 25-28 based on Chapel et al. under 35 U.S.C. § 102(b).

Morell et al.

The Examiner has rejected claims 1-3, 7-11, 25 and 28 under 35 U.S.C. § 102(b) based on Morell et al.* Applicants traverse.

Like Chapel et al., Morell et al. does not provide any evidence that metastatic lymphoma was present at the time of IVIG administration. For all of the reasons set forth above regarding the deficiency of the evidence supporting a case of inherent anticipation by Chapel et al., Morell et al. does not anticipate the pending claims.

Thus, applicants respectfully request that the Examiner withdraw the rejection of claims 1-3, 7-11, 25 and 28 based on Morell et al. under 35 U.S.C. § 102(b).

* A. Morell and S. Barandun, "Prophylactic and Therapeutic Use of Immunoglobulin for Intravenous Administration in Patients with Secondary Immunodeficiencies Associated with Malignancies," Pediat. Infect. Dis. J. 7, pp. S87-S91 (1988).

Besa et al.

The Examiner has rejected claims 1-3, 6-9 and 25-28 under 35 U.S.C.

§ 102(b) based on Besa et al.* Applicants traverse.

Like Chapel et al. and Morell et al., Besa et al. does not provide any evidence that metastatic lymphoma was present at the time of IVIG administration. For all of the reasons set forth above regarding the deficiency of the evidence supporting a case of inherent anticipation by Chapel et al., Besa et al. does not anticipate the pending claims.

Thus, applicants respectfully request that the Examiner withdraw the rejection of claims 1-3, 6-9 and 25-28 based on Besa et al. under 35 U.S.C. § 102(b).

Vitetta et al.

The Examiner has rejected claim 29 under 35 U.S.C. § 102(b) in view of Vitetta et al. The Examiner asserts that Vitetta et al.** administered immunoglobulin to lymphoma patients intravenously, thereby anticipating the claimed invention. Applicants traverse.

Vitetta et al. disclose the use of the Fab' fragment of a monoclonal anti-CD22 antibody (RFB4) coupled to chemically deglycosylated ricin A chain. This is not IVIG as defined in applicants' specification. Applicants have defined "IVIG" as "gamma globulin preparations suitable for intravenous use, such as those IVIG preparations commercially

* Besa et al., Am. J. Med. 84, pp. 691-698 (1988).

** Vitetta et al., Cancer Research, Vol. 51, pp. 4052-4058 (1991).

available from several sources,” and “gamma globulin” is defined as “the serum globulin fraction that is mainly composed of IgG molecules.” (specification at page 4, lines 13-18). The serum gamma globulin fraction, by definition, is not a monoclonal antibody fraction. One of skill in the art would have understood from these definitions and from the examples of the specification that IVIG is a term of art that refers to preparations of the serum gammaglobulin fraction of broad specificity suitable for intravenous use (see also specification at page 5, lines 5-19). IVIG would have been understood **not** to comprise preparations of individual monoclonal antibodies as used in Vitetta et al.

Monoclonal antibody preparations, by definition, have a very narrow specificity. IVIG, in contrast, is a pool of immunoglobulins prepared from human serum that has an extremely broad specificity. The concept of a monoclonal antibody preparation is fundamentally incompatible with the concept of an immunoglobulin G preparation. One of skill in the art would have known as of the filing date of the instant invention that IVIG is not a monoclonal antibody preparation. One of skill in the art would have understood that the Fab’ fragments referred to in Vitetta et al. were not an Fab’ fragment preparation of IVIG.

In summary, Vitetta et al. does not anticipate the instant invention because IVIG is not used in the study. Vitetta et al. also does not inherently anticipate the claimed invention, for the reasons enumerated above in applicants’ discussion of Chapel et al., Morell et al. and Besa et al. Specifically, Vitetta et al. does not definitively disclose inhibition of metastasis of lymphoma or treatment of metastatic lymphoma. Applicants

therefore respectfully request that the Examiner withdraw the rejection of claim 29 based on Vitetta et al. under 35 U.S.C. § 102(b).

Double Patenting

Claims 1-11 and 22-29 stand rejected as unpatentable over issued claims 1-18 of U.S. patent 5,965,130 and issued claims 1-10 of U.S. patent 5,562,902 under the obviousness-type double patenting doctrine. Applicants remain ready to submit a terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) upon an indication by the Examiner that all other rejections are withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph

Pending claims 22-29 stand rejected under 35 U.S.C. § 112, second paragraph as being “vague and indefinite in the recitation of ‘A method for treating lymphoma in a mammal which comprises’” The Examiner also states “[w]ithout a clear definition as to what criterium is being measured one of skill in the art would be unable to ascertain the metes and bounds of ‘treating’.” Applicants traverse.

The claim term “treating” is a commonly used word with an ordinary meaning that would have been known to one of skill in the art as of the filing date of the application. For example, the American Heritage Dictionary defined the verb “treat” as “[t]o give medical aid to counteract (a disease or condition)” (definition 7b.). The American Heritage Dictionary, 3d Ed., Houghton Mifflin Co.:Boston, p. 1906 (1996). There is no

need to further define the term "treat" by listing criteria, because one of skill in the art would have understood the term adequately in the context of the claims and the specification. In view of the above remarks, applicants respectfully request that the Examiner withdraw the rejection of claims 22-29 under 35 U.S.C. § 112, second paragraph.

For all of the above reasons, applicants submit that each of the pending claims are now in condition for allowance and request that this application be passed to issue. However, if the Examiner believes that an interview would facilitate the resolution of any outstanding issue, the Examiner is kindly requested to contact the undersigned.

Respectfully submitted,



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